

App. No. 10/027,404
Amtd. dated November 30, 2004
Reply to Office Action of July 1, 2004

PATENT

REMARKS/ARGUMENTS

I. Claim Status and Related Applications

Claims 1-6 and 50-94 are under examination.¹

Applicants wish to advise the Examiner of the following related patents and patent applications:

Application No. (Filing Date)	Status
09/562195 (05/01/2000)	Granted (U.S. Pat. No. 6,783,934)
09/808674 (03/14/2001)	Granted (U.S. Pat. No. 6,713,297)
09/808706 (03/14/2001)	Pending
09/808877 (03/14/2001)	Abandoned
10/702538 (11/05/2003)	Pending

II. Request for Removal of Finality

The Office Action mailed July 1, 2004, was identified as a final action. A final action is improper where there is a new ground of rejection introduced by the examiner, unless the new ground was necessitated by amendment to the claims and/or was based on information submitted in an information disclosure statement filed under 37 CFR 1.97(c). *See* M.P.E.P. §§ 706.07(a), 706.07(c) and 706.07(d). In the present case, not only is a new ground of rejection raised in the Office Action; *all* of the rejections are new. Further, the rejections cannot be said to be necessitated by the amendments made by Applicants. For example, the amendment to Claim 1, adding the phrases "at least one" and "the threshold" to is wholly unrelated to the various rejections newly made by the Office.

Accordingly, Applicants respectfully request that the finality of the Office Action mailed July 1, 2004, be withdrawn.

¹ The Office indicated in several places that claims 1-5 and 50-94 were rejected on various grounds. For purposes of this response, Applicants have assumed the Office intended to include Claim 6 in each rejection.

III. Objection to Specification

The Office objects to the incorporation by reference of PCT Publication WO 99/48608. The Office asserts that the incorporation is improper because Applicants allegedly have failed to teach what part of the reference is referred to. The Office relies on based on *Advanced Display Systems v. Kent State Univ.* 54 USPQ2d 1673 (CAFC 2000) for this position.

Applicants specifically explain that WO 99/48608 is referenced for teaching a modified version of PID control. The modified PID control is discussed in the specification in detail. *See, e.g.,* page 66, line 26 to page 67, line 17. Further, it is entirely proper in an incorporation by reference to refer to the entire document. See MPEP 2163.07, "an application may attempt to incorporate the ***content of another document or part thereof*** by reference to the document in the text of the specification" (emphasis added). Accordingly, the incorporation by reference is proper. Applicants respectfully request this objection be withdrawn.

Advanced Display Systems, relied on by the Office, is inapposite to the present case. In *Advanced Display Systems* the question was whether a prior art patent could be an anticipatory reference based on elements not literally found in the patent, but described in a publication incorporated by reference into the patent. This is not the situation in the instant case. Further, the *Advanced Display Systems* court made clear that in making a determination "whether and to what extent material has been incorporated by reference" "the standard of one reasonably skilled in the art should be used to determine whether the host document describes the material to be incorporated by reference with sufficient particularity." *Advanced Display Systems* at 1680. One reasonably skilled in the art would find the specification reference to the PID control of WO 99/48608 sufficiently clear.

IV. Rejections Citing 35 USC 112, First Paragraph (Written Description)

Claims 1-5 and 50-94 stand rejected under 35 U.S.C. 112, First Paragraph as allegedly failing to comply with the written description requirement.

A. Rejection Articulated in Paragraph 7 of the Office Action

As applicants understand this rejection, the Office asserts the specification does not adequately describe an apparatus for determining the threshold cycle number of application where "the device comprises but these two elements." As applicants understand it, the Office believes that the claims must recite at least four elements: (a) the recited detection mechanism; (b) the recited controller; (c) an element that can be detected by the detection mechanism and (d) an element over which the controller exerts control. As Applicants understand the rejection, an example of an element that can be detected by the detection mechanism would be a reaction vessel containing components of an amplification reaction, and an example of an element over which the controller exerts control would be a thermal cycler. Applicants respectfully traverse this rejection.

The Office appears to construe Applicants' claims as directed to **"An apparatus that carries out an amplification reaction."** However, the claims are not directed to an apparatus that, in and of itself, necessarily carries out an amplification reaction. The claims under examination are directed to "An apparatus for determining a threshold cycle number in a nucleic acid amplification reaction." The claimed device, comprising a detector and a controller, is sufficient for determining a threshold cycle number. Applicants note, without intending to limit the invention, that for carrying out an amplification reaction the claimed apparatus can be used in conjunction with other devices or elements. For example, the claimed device can be used with any of a variety of reaction vessels (e.g., the detector of the apparatus can be positioned near a nucleic acid reaction mixture). Similarly, the claimed device can be used in conjunction with a variety of types of thermal cyclers or other elements, and/or the threshold cycle number can be stored in memory. However, neither a reaction vessel nor a thermal cycler is a necessary component of the claimed apparatus *per se*. It is clear that determination of a threshold cycle number in a nucleic acid amplification reaction does not require that the controller exert control

over an aspect of the apparatus. See, for example, page 98, lines 14-15 of the specification explaining that "FIG. 46 is a table showing the threshold values computed by the controller" Clearly, the threshold values are determined before and without the necessity of control over a thermal cycler or other element. The open language of the claim contemplates, of course, that in certain embodiments the apparatus may include a vessel and/or an element acted on by the controller.

Applicants further note that an apparatus comprising a detector and a controller is recited in the claims as originally filed (*e.g.*, original claim 1). As explained in the Manual of Patent Examining Procedure, "There is a strong presumption that an adequate written description of the invention is present in the specification as filed. Consequently, rejection of an original claim for lack of written description should be rare." See MPEP 2163 II(A) (page 2100-168 of the May 2004 edition, citing *In re Wertheim* 191 USPQ 90 (CCPA 1976))

Accordingly, Applicants respectfully submit that the claimed apparatus is fully described, and that the rejection under § 112, first paragraph, should be withdrawn.

B Rejection Articulated in Paragraph 8 of the Office Action

As a second basis for rejection under Section 112, first paragraph, the Office states in paragraph 8 of the action "As presently worded, the claimed apparatus could comprise a reaction vessel of virtually any size." Applicants again emphasize that the claimed apparatus for determining a threshold cycle number in a nucleic acid amplification reaction is used in conjunction with a reaction vessel, but the vessel need not necessarily be a part of the apparatus.

The Office goes on to state the specification "does not reasonably support a device that comprises an infinite number of elements" Applicants agree with the Office. Similarly, the Office states the specification "does not reasonably support a device . . . where the reaction chamber of the apparatus can be of virtually [any?] dimension." Applicants again agree. During examination the Office must give claims their broadest reasonable interpretation. See MPEP 2111.01. To suggest that the claims are directed to a device that comprises an infinite number of elements is to misconstrue the open (comprising) language of the claim and is not a *reasonable* interpretation of the claim. Similarly, to suggest that the reaction chamber of the apparatus can

be of virtually any dimension is not *reasonable*; nor is it relevant, given that the claim does not recite a reaction vessel. Applicants respectfully request that this rejection be withdrawn.

Finally, the Office asserts that page 28, last paragraph, of the specification, teaches that a vessel must be of particular dimensions. However, this section of the specification clearly states that these particular dimensions are "preferred." It has been long established by the courts that an applicant is not limited to claiming the preferred embodiment. This must particularly be the case when, as here, the Applicants provided an abundance of examples and alternatives.²

V. Rejections Citing 35 USC 112, First Paragraph (Enablement)

Claims 1-5 and 50-94 were rejected as not enabled.

In articulating this enablement rejection the Office states "the specification does not provide an adequate written description of the apparatus." Applicants have addressed the written description rejection above in Section IV.

The Office further states "the specification has not been found to set forth a reproducible procedure whereby the claimed apparatus would be able to accurately determine any threshold number of cycles of nucleic acid amplification are to be performed [sic] where there is but one amplicon to be produced." Insofar as the pending claims are to an apparatus, and not to a method or procedure, Applicants interpret the Office's comments as an assertion that the device

² On the contrary, the specification provides abundant description of reaction vessels and notes:

"An engineer having ordinary skill in the art will be able to select suitable values for the volumes V_1 and V_2 using the description and equation given above. . . "

"This is just one example of suitable dimensions for the vessel 12 and is not intended to limit the scope of the invention. Many other suitable values may be selected."

"In selecting suitable dimensions for the channel 28 and pressure stroke distance D_3 (and thus the volumes V_1 , V_2), there is no theoretical limit to how large or small the dimensions may be. It is only important that the ratio of the volumes $V_1:V_2$ yield the desired final desired pressure P_2 in the chamber."

"Further, the specialized reaction vessels described above are preferred, but the apparatus and methods of the present invention are applicable to any type of vessel including plastic reaction tubes, glass capillary tubes, microtiter plates, cartridges or cuvettes, etc. "

See the specification at page 23, lines 21-24; page 24, lines 7-10; page 24, lines 1-16; and page 102, lines 17-22, respectfully.)

does not work, or at least does not work "accurately," for every conceivable type of amplification reaction. There is no basis in the law for requiring a device work for all purposes or under all conditions. Accordingly, even if, *arguendo*, the assertion of the Office had merit, it is irrelevant to the patentability of the pending claims. One of ordinary skill in the art, guided by Applicants' disclosure, would understand how, and for what purposes, the claimed device should be used.

For the reasons give above, Applicants respectfully request this rejection be withdrawn.³

VI. Rejection Under 35 USC 112, Second Paragraph

The Office states the claims are incomplete for omitting essential elements, such omission amounting to a gap between the elements. The allegedly omitted elements are those that "permit the artisan to control the various aspects of the cycles of amplification, *e.g.*, temperature, duration, temperature ramp time, volume of reagents, frequency of measurement, communication means between the controller and the elements to be controlled."

Again, Applicants respectfully submit this rejection is premised on misconstruction of the claims. The claimed invention is to an apparatus for determining a threshold cycle number. The claimed device does not require elements to, for example, control the "volume of reagents."⁴

The Office is respectfully asked to withdraw this rejection.

VII. Rejection Under 35 USC §101

Claims 1-5 and 50-94 were rejected as allegedly lacking utility. The rationale for the rejection is that the claimed apparatus is "void of any reaction chamber, or communicating means that would allow for measurement, much less control of the detection mechanism." As

³ The Office refers, in this enablement rejection, to the "unpredictable nature of the art to which the claimed invention is directed . . ." In the event the rejection is maintained, Applicants respectfully request clarification. The invention is an apparatus. Inventions having mechanical or electrical elements are generally considered to involve predictable factors. See *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970) and *In re Cook* 169 USPQ 298, 301 (CCPA 1971).

explained above in Section IV, the present claims are directed to an apparatus for determining a threshold cycle number in a nucleic acid amplification reaction, the apparatus comprising at least one detection mechanism for measuring, at a plurality of different times during the amplification reaction, at least one signal whose intensity is related to the quantity of a nucleic acid sequence being amplified in the reaction; and an appropriately programmed controller in communication with the detection mechanism. Although the open language of the claim encompasses an apparatus that also comprises a reaction vessel, the absence of such a vessel does not render the apparatus inoperative or, as asserted by the Office, establish that it "is not possible for the claimed apparatus to function in a manner set forth in the preamble of the claims." As discussed above, the claimed apparatus is sufficient to determine a threshold cycle number in a nucleic acid amplification reaction.

For the reasons discussed above, Applicants respectfully request this rejection be withdrawn.

VIII. Double Patenting

Claims 1-5 and 50-94 were rejected under the doctrine of obviousness-type double patenting over claims 1-48 of U.S. Patent No. 6,713,297 ("the '297 patent"). The Office states that the claims "are not patentably distinct from each other because both sets of claims are drawn to an apparatus comprising at least one detection mechanism and at least one controller where the controller has been programmed to measure the amount of nucleic acid template present in a sample and to determine the threshold cycle number." Applicants respectfully traverse.

The claims of the '297 patent are directed to an apparatus with a controller programmed to use quantitative internal controls for quantitation of nucleic acids and not, as stated by the Office, to determine threshold cycle number. In contrast, the instant claims are directed to an apparatus comprising a controller programmed to determine the threshold cycle number from a derivative of the growth curve and does not necessarily relate to internal controls. To establish a

⁴ Although the Office listed the allegedly omitted elements, the Office provided no rationale for considering the omitted elements critical or essential as required. See MPEP 706.03(d). If this rejection is maintained, clarification is requested.

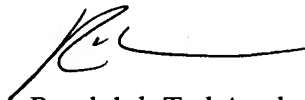
prima facie case of obviousness-type double patenting the Office must set forth the basis for alleged obviousness, including the reasons a person of ordinary skill in the art would conclude that the invention defined in the claim at issue is an obvious variation of the invention defined in a claim of the patent. The Office has not presented such an argument. See MPEP 804(II)(b)(1). The Office has merely stated, incorrectly, that the claims of instant application and '297 patent are drawn to the same apparatus. Accordingly, Applicants respectfully request this rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes there are any remaining issues, please call the undersigned applicant's representative at 650-326-2400 in order to expedite prosecution.

Respectfully submitted,



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